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<110> EXELIXIS, INC.

<120> RABS AS MODIFIERS OF THE p53 PATHWAY AND METHODS OF USE

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<150> US 60/394,992

<151> 2002-07-10

<150> US 60/410,988

<151> 2002-09-16

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Glu Val Met Val Asp Asp Arg Leu Val Thr Met Gln Ile Trp Asp Thr
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Ala Gly Gln Glu Arg Phe Gln Ser Leu Gly Val Ala Phe Tyr Arg Gly
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Ala Asp Cys Cys Val Leu Val Phe Asp Val Thr Ala Pro Asn Thr Phe
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Lys Thr Leu Asp Ser Trp Arg Asp Glu Phe Leu Val Gln Ala Ser Pro
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Arg Asp Pro Glu Asn Phe Pro Phe Val Val Leu Gly Asn Lys Val Asp
115 120 125

Leu Glu Asn Arg Gln Val Ala Thr Lys Arg Ala Gln Ala Trp Cys Tyr
130 135 140

Ser Lys Asn Asn Ile Pro Tyr Phe Glu Thr Ser Ala Lys Glu Ala Ile
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Asn Val Glu Gln Ala Phe Gln Thr Ile Ala Arg Asn Ala Leu Lys Gln
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<400> 33

Met Thr Ser Arg Lys Lys Val Leu Leu Lys Val Ile Ile Leu Gly Asp
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Ser Gly Val Gly Lys Thr Ser Leu Met Asn Gln Tyr Val Asn Lys Lys
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Phe Ser Asn Gln Tyr Lys Ala Thr Ile Gly Ala Asp Phe Leu Ile Lys
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Glu Val Met Val Asp Asp Arg Leu Val Thr Met Gln Ile Trp Asp Thr
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Gly Gly Gln Glu Arg Phe Arg Ser Met Val Ser Thr Phe Tyr Lys Gly
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115 120 125

Ala Asp Arg Lys Val Pro Gln Glu Val Ala Gln Gly Trp Cys Arg Glu
130 135 140

Lys Asp Ile Pro Tyr Phe Glu Val Ser Ala Lys Asn Asp Ile Asn Val
145 150 155 160

Val Gln Ala Phe Glu Met Leu Ala Ser Arg Ala Leu Ser Arg Tyr Gln
165 170 175

Ser Ile Leu Glu Asn His Leu Thr Glu Ser Ile Lys Leu Ser Pro Asp
180 185 190

Gln Ser Arg Ser Arg Cys Cys
195

<210> 35
<211> 201
<212> PRT
<213> Homo sapiens

<400> 35

Met Ala Gly Lys Ser Ser Leu Phe Lys Val Ile Leu Leu Gly Asp Gly
1 5 10 15

Gly Val Gly Lys Ser Ser Leu Met Asn Arg Tyr Val Thr Asn Lys Phe
20 25 30

Asp Thr Gln Leu Phe His Thr Ile Gly Val Glu Phe Leu Asn Lys Asp
35 40 45

Leu Glu Val Asp Gly His Phe Val Thr Met Gln Ile Trp Asp Thr Ala
50 55 60

Gly Gln Glu Arg Phe Arg Ser Leu Arg Thr Pro Phe Tyr Arg Gly Ser
65 70 75 80

Asp Cys Cys Leu Leu Thr Phe Ser Val Asp Asp Ser Gln Ser Phe Gln
85 90 95

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Asn Leu Ser Asn Trp Lys Lys Glu Phe Ile Tyr Tyr Ala Asp Val Lys
100 105 110

Glu Pro Glu Ser Phe Pro Phe Val Ile Leu Gly Asn Lys Ile Asp Ile
115 120 125

Ser Glu Arg Gln Val Ser Thr Glu Glu Ala Gln Ala Trp Cys Arg Asp
130 135 140

Asn Gly Asp Tyr Pro Tyr Phe Glu Thr Ser Ala Lys Asp Ala Thr Asn
145 150 155 160

Val Ala Ala Ala Phe Glu Glu Ala Val Arg Arg Val Leu Ala Thr Glu
165 170 175

Asp Arg Ser Asp His Leu Ile Gln Thr Asp Thr Val Asn Leu His Arg
180 185 190

Lys Pro Lys Pro Ser Ser Ser Cys Cys
195 200

<210> 36
<211> 201
<212> PRT
<213> Homo sapiens

<400> 36

Met Ser Gly Lys Ser Leu Leu Leu Lys Val Ile Leu Leu Gly Asp Gly
1 5 10 15

Gly Val Gly Lys Ser Ser Leu Met Asn Arg Tyr Val Thr Asn Lys Phe
20 25 30

Asp Ser Gln Ala Phe His Thr Ile Gly Val Glu Phe Leu Asn Arg Asp
35 40 45

Leu Glu Val Asp Gly Arg Phe Val Thr Leu Gln Ile Trp Asp Thr Ala
50 55 60

Gly Gln Glu Arg Phe Lys Ser Leu Arg Thr Pro Phe Tyr Arg Gly Ala
65 70 75 80

Asp Cys Cys Leu Leu Thr Phe Ser Val Asp Asp Arg Gln Ser Phe Glu
85 90 95

Asn Leu Gly Asn Trp Gln Lys Glu Phe Ile Tyr Tyr Ala Asp Val Lys
100 105 110

EX03-050C-US.patentin.txt

Asp Pro Glu His Phe Pro Phe Val Val Leu Gly Asn Lys Val Asp Lys
115 120 125

Glu Asp Arg Gln Val Thr Thr Glu Glu Ala Gln Thr Trp Cys Met Glu
130 135 140

Asn Gly Asp Tyr Pro Tyr Leu Glu Thr Ser Ala Lys Asp Asp Thr Asn
145 150 155 160

Val Thr Val Ala Phe Glu Glu Ala Val Arg Gln Val Leu Ala Val Glu
165 170 175

Glu Gln Leu Glu His Cys Met Leu Gly His Thr Ile Asp Leu Asn Ser
180 185 190

Gly Ser Lys Ala Gly Ser Ser Cys Cys
195 200

<210> 37
<211> 215
<212> PRT
<213> Homo sapiens

<400> 37

Met Ala Ser Arg Gly Ala Thr Arg Pro Asn Gly Pro Asn Thr Gly Asn
1 5 10 15

Lys Ile Cys Gln Phe Lys Leu Val Leu Leu Gly Glu Ser Ala Val Gly
20 25 30

Lys Ser Ser Leu Val Leu Arg Phe Val Lys Gly Gln Phe His Glu Phe
35 40 45

Gln Glu Ser Thr Ile Gly Ala Ala Phe Leu Thr Gln Thr Val Cys Leu
50 55 60

Asp Asp Thr Thr Val Lys Phe Glu Ile Trp Asp Thr Ala Gly Gln Glu
65 70 75 80

Arg Tyr His Ser Leu Ala Pro Met Tyr Tyr Arg Gly Ala Gln Ala Ala
85 90 95

Ile Val Val Tyr Asp Ile Thr Asn Glu Glu Ser Phe Ala Arg Ala Lys
100 105 110

Asn Trp Val Lys Glu Leu Gln Arg Gln Ala Ser Pro Asn Ile Val Ile
115 120 125

Ala Leu Ser Gly Asn Lys Ala Asp Leu Ala Asn Lys Arg Ala Val Asp
 130 135 140

Phe Gln Glu Ala Gln Ser Tyr Ala Asp Asp Asn Ser Leu Leu Phe Met
 145 150 155 160

Glu Thr Ser Ala Lys Thr Ser Met Asn Val Asn Glu Ile Phe Met Ala
 165 170 175

Ile Ala Lys Lys Leu Pro Lys Asn Glu Pro Gln Asn Pro Gly Ala Asn
 180 185 190

Ser Ala Arg Gly Arg Gly Val Asp Leu Thr Glu Pro Thr Gln Pro Thr
 195 200 205

Arg Asn Gln Cys Cys Ser Asn
 210 215

<210> 38
 <211> 216
 <212> PRT
 <213> Homo sapiens

<400> 38

Met Ala Gly Arg Gly Gly Ala Arg Arg Pro Asn Gly Pro Ala Ala Gly
 1 5 10 15

Asn Lys Ile Cys Gln Phe Lys Leu Val Leu Leu Gly Glu Ser Ala Val
 20 25 30

Gly Lys Ser Ser Leu Val Leu Arg Phe Val Lys Gly Gln Phe His Glu
 35 40 45

Tyr Gln Glu Ser Thr Ile Gly Ala Ala Phe Leu Thr Gln Thr Val Cys
 50 55 60

Leu Asp Asp Thr Thr Val Lys Phe Glu Ile Trp Asp Thr Ala Gly Gln
 65 70 75 80

Glu Arg Tyr His Ser Leu Ala Pro Met Tyr Tyr Arg Gly Ala Gln Ala
 85 90 95

Ala Ile Val Val Tyr Asp Ile Thr Asn Thr Asp Thr Phe Ala Arg Ala
 100 105 110

Lys Asn Trp Val Lys Glu Leu Gln Arg Gln Ala Ser Pro Asn Ile Val
 115 120 125

EX03-050C-US.patentin.txt

Ile Ala Leu Ala Gly Asn Lys Ala Asp Leu Ala Ser Lys Arg Ala Val
130 135 140

Glu Phe Gln Glu Ala Gln Ala Tyr Ala Asp Asp Asn Ser Leu Leu Phe
145 150 155 160

Met Glu Thr Ser Ala Lys Thr Ala Met Asn Val Asn Glu Ile Phe Met
165 170 175

Ala Ile Ala Lys Lys Leu Pro Lys Asn Glu Pro Gln Asn Ala Thr Gly
180 185 190

Ala Pro Gly Arg Asn Arg Gly Val Asp Leu Gln Glu Asn Asn Pro Ala
195 200 205

Ser Arg Ser Gln Cys Cys Ser Asn
210 215

<210> 39
<211> 215
<212> PRT
<213> Homo sapiens

<400> 39

Met Thr Ser Arg Ser Thr Ala Arg Pro Asn Gly Gln Pro Gln Ala Ser
1 5 10 15

Lys Ile Cys Gln Phe Lys Leu Val Leu Leu Gly Glu Ser Ala Val Gly
20 25 30

Lys Ser Ser Leu Val Leu Arg Phe Val Lys Gly Gln Phe His Glu Tyr
35 40 45

Gln Glu Ser Thr Ile Gly Ala Ala Phe Leu Thr Gln Ser Val Cys Leu
50 55 60

Asp Asp Thr Thr Val Lys Phe Glu Ile Trp Asp Thr Ala Gly Gln Glu
65 70 75 80

Arg Tyr His Ser Leu Ala Pro Met Tyr Tyr Arg Gly Ala Gln Ala Ala
85 90 95

Ile Val Val Tyr Asp Ile Thr Asn Gln Glu Thr Phe Ala Arg Ala Lys
100 105 110

Thr Trp Val Lys Glu Leu Gln Arg Gln Ala Ser Pro Ser Ile Val Ile
115 120 125

EX03-050C-US.patentin.txt

Ala Leu Ala Gly Asn Lys Ala Asp Leu Ala Asn Lys Arg Met Val Glu
130 135 140

Tyr Glu Glu Ala Gln Ala Tyr Ala Asp Asp Asn Ser Leu Leu Phe Met
145 150 155 160

Glu Thr Ser Ala Lys Thr Ala Met Asn Val Asn Asp Leu Phe Leu Ala
165 170 175

Ile Ala Lys Lys Leu Pro Lys Ser Glu Pro Gln Asn Leu Gly Gly Ala
180 185 190

Ala Gly Arg Ser Arg Gly Val Asp Leu His Glu Gln Ser Gln Gln Asn
195 200 205

Lys Ser Gln Cys Cys Ser Asn
210 215

<210> 40
<211> 194
<212> PRT
<213> Homo sapiens

<400> 40

Met Ala Leu Arg Glu Leu Lys Val Cys Leu Leu Gly Asp Thr Gly Val
1 5 10 15

Gly Lys Ser Ser Ile Val Trp Arg Phe Val Glu Asp Ser Phe Asp Pro
20 25 30

Asn Ile Asn Pro Thr Ile Gly Ala Ser Phe Met Thr Lys Thr Val Gln
35 40 45

Tyr Gln Asn Glu Leu His Lys Phe Leu Ile Trp Asp Thr Ala Gly Gln
50 55 60

Glu Arg Phe Arg Ala Leu Ala Pro Met Tyr Tyr Arg Gly Ser Ala Ala
65 70 75 80

Ala Ile Ile Val Tyr Asp Ile Thr Lys Glu Glu Thr Phe Ser Thr Leu
85 90 95

Lys Asn Trp Val Lys Glu Leu Arg Gln His Gly Pro Pro Asn Ile Val
100 105 110

Val Ala Ile Ala Gly Asn Lys Cys Asp Leu Ile Asp Val Arg Glu Val
115 120 125

EX03-050C-US.patentin.txt

Met Glu Arg Asp Ala Lys Asp Tyr Ala Asp Ser Ile His Ala Ile Phe
130 135 140

Val Glu Thr Ser Ala Lys Asn Ala Ile Asn Ile Asn Glu Leu Phe Ile
145 150 155 160

Glu Ile Ser Arg Arg Ile Pro Ser Thr Asp Ala Asn Leu Pro Ser Gly
165 170 175

Gly Lys Gly Phe Lys Leu Arg Arg Gln Pro Ser Glu Pro Lys Arg Ser
180 185 190

Cys Cys

<210> 41
<211> 212
<212> PRT
<213> Homo sapiens
<400> 41

Met Ala Gln Ala His Arg Thr Pro Gln Pro Arg Ala Ala Pro Ser Gln
1 5 10 15

Pro Arg Val Phe Lys Leu Val Leu Leu Gly Ser Gly Ser Val Gly Lys
20 25 30

Ser Ser Leu Ala Leu Arg Tyr Val Lys Asn Asp Phe Lys Ser Ile Leu
35 40 45

Pro Thr Val Gly Cys Ala Phe Phe Thr Lys Val Val Asp Val Gly Ala
50 55 60

Thr Ser Leu Lys Leu Glu Ile Trp Asp Thr Ala Gly Gln Glu Lys Tyr
65 70 75 80

His Ser Val Cys His Leu Tyr Phe Arg Gly Ala Asn Ala Ala Leu Leu
85 90 95

Val Tyr Asp Ile Thr Arg Lys Asp Ser Phe Leu Lys Ala Gln Gln Trp
100 105 110

Leu Lys Asp Leu Glu Glu Glu Leu His Pro Gly Glu Val Leu Val Met
115 120 125

Leu Val Gly Asn Lys Thr Asp Leu Ser Gln Glu Arg Glu Val Thr Phe
130 135 140

EX03-050C-US.patentin.txt

Gln Glu Gly Lys Glu Phe Ala Asp Ser Gln Lys Leu Leu Phe Met Glu
145 150 155 160

Thr Ser Ala Lys Leu Asn His Gln Val Ser Glu Val Phe Asn Thr Val
165 170 175

Ala Gln Glu Leu Leu Gln Arg Ser Asp Glu Glu Gly Gln Ala Leu Arg
180 185 190

Gly Asp Ala Ala Val Ala Leu Asn Lys Gly Pro Ala Arg Gln Ala Lys
195 200 205

Cys Cys Ala His
210

<210> 42
<211> 194
<212> PRT
<213> Homo sapiens
<400> 42

Met Ala Ile Arg Glu Leu Lys Val Cys Leu Leu Gly Asp Thr Gly Val
1 5 10 15

Gly Lys Ser Ser Ile Val Cys Arg Phe Val Gln Asp His Phe Asp His
20 25 30

Asn Ile Ser Pro Thr Ile Gly Ala Ser Phe Met Thr Lys Thr Val Pro
35 40 45

Cys Gly Asn Glu Leu His Lys Phe Leu Ile Trp Asp Thr Ala Gly Gln
50 55 60

Glu Arg Phe His Ser Leu Ala Pro Met Tyr Tyr Arg Gly Ser Ala Ala
65 70 75 80

Ala Val Ile Val Tyr Asp Ile Thr Lys Gln Asp Ser Phe Tyr Thr Leu
85 90 95

Lys Lys Trp Val Lys Glu Leu Lys Glu His Gly Pro Glu Asn Ile Val
100 105 110

Met Ala Ile Ala Gly Asn Lys Cys Asp Leu Ser Asp Ile Arg Glu Val
115 120 125

Pro Leu Lys Asp Ala Lys Glu Tyr Ala Glu Ser Ile Gly Ala Ile Val
130 135 140

EX03-050C-US.patentin.txt

Val Glu Thr Ser Ala Lys Asn Ala Ile Asn Ile Glu Glu Leu Phe Gln
145 150 155 160

Gly Ile Ser Arg Gln Ile Pro Pro Leu Asp Pro His Glu Asn Gly Asn
165 170 175

Asn Gly Thr Ile Lys Val Glu Lys Pro Thr Met Gln Ala Ser Arg Arg
180 185 190

Cys Cys